NEW JERSEY DEPARTMENT OF HEALTH & SENIOR SERVICES

NEW JERSEY GUIDE TO POST-EXPOSURE RABIES PROPHYLAXIS FOR THE HEALTH CARE PROFESSIONAL
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BACKGROUND

Raccoon rabies entered New Jersey in the fall of 1989 and has since spread throughout the entire State and continues to create a threat to residents and their domestic animals. Although approximately 75 percent of the animals confirmed to be rabid through laboratory testing are raccoons, many other animals (especially skunks, groundhogs, foxes, and free-roaming cats) also have become infected after exposure to raccoons. The Department estimates that approximately 2,000 people receive rabies post-exposure prophylaxis annually due to exposure to rabid or suspect rabid animals.

Once symptoms of rabies develop, there is no known effective prophylaxis for the disease. Fortunately, the available rabies biologics (human rabies immune globulin and human rabies vaccine) are effective in preventing rabies, if given in a timely manner following exposure to a rabid animal. This guide will review rabies post-exposure prophylaxis and associated frequently asked questions. Please review it and keep it as a reference.

WHAT AM I LEGALLY REQUIRED TO DO?

Every physician is legally required to report all animal bites and all administrations of human post-exposure rabies prophylaxis to the **local health agencies** with jurisdiction where the person resides within 12 hours of initial medical treatment (N.J.R.S. 26:4-79). The local health agency with jurisdiction over the exposed person will work with other agencies as required to oversee administration of post-exposure prophylaxis and test or confine suspect animals, if indicated. The telephone number for local health agencies can be found under the municipal listing in the telephone book or on-line at http://www.state.nj.us/health/lh/directory/lhdselectcounty.htm. A form to report rabies post-exposure prophylaxis is available on-line at these links: (PDF 40K) (Word 60K)

WHAT ASSISTANCE DOES THE STATE OFFER?

Representatives of the Department's Infectious and Zoonotic Diseases Program are available to assist physicians in making prophylaxis decisions by calling (609) 588-3121 or 588-7500 between 8 a.m. and 5 p.m. on workdays. Department on-call staff can be reached during nights, weekends, and holidays by calling (609) 392-2020.

All local health departments have been supplied with a detailed rabies decision-making algorithm and are also available for consultation.

WHO NEEDS TO RECEIVE RABIES POST-EXPOSURE PROPHYLAXIS?

The following are important considerations in determining the need for prophylaxis:

1. Was there an exposure - bite or nonbite?

The following section is from the Advisory Committee Immunization Practices (ACIP) Recommendations (1):

"Rabies is transmitted only when the virus is introduced into bite wounds or open cuts in skin or onto mucous membranes. If there has been no exposure (i.e., no bite or nonbite exposure), post-exposure prophylaxis is not necessary. The likelihood of rabies infection varies with the nature and extent of exposure. Two categories of exposure (bite and nonbite) should be considered:

> Bite - Any penetration of the skin by teeth constitutes a bite exposure. Bites, regardless of location, represent a potential risk of rabies transmission. Bites by some animals, such as bats, can inflict minor injury and thus be undetected.
>
> Nonbite – Nonbite exposures from terrestrial animals rarely cause rabies. However, occasional reports of transmission by nonbite exposure suggest that such exposures constitute sufficient reason to consider post-exposure prophylaxis. The nonbite exposures of highest risk appear to be among persons exposed to large amounts of aerosolized rabies virus and surgical recipients of corneas transplanted from patients who died of rabies. Two cases of rabies have been attributed to probable aerosol exposures in laboratories, and two cases of rabies have been attributed to possible airborne exposure in caves containing millions of free-tailed bats (*Tadarida brasiliensis*) in the Southwest.
>
> The contamination of open wounds, abrasions, mucous membranes, or theoretically, scratches, with saliva or other potentially infectious material (such as neural tissue) from a rabid animal also constitutes a nonbite exposure. Other contact by itself, such as petting a rabid animal and contact with the blood, urine, or feces (e.g., guano) of a rabid animal, does not constitute an exposure and is not an indication for prophylaxis. Because the rabies virus is inactivated by desiccation and ultraviolet irradiation, in general, if the material containing the virus is dry, the virus can be considered noninfectious."

2. What type of animal was involved? Refer to section:

Dog or cat	3
Bat, raccoon, skunk, fox, & other wild carnivorous animals	4
Woodchuck/groundhog	4
Rodents (other than groundhog)	5
Lagomorphs (rabbits and hares)	5
Ferrets and other exotic pets	6
Livestock/Other	6

3. Is the dog or cat available for observation?

YES - Animal Available

<u>IF HEALTHY</u>, DOGS OR CATS (BOTH VACCINATED AND UNVACCINATED FOR RABIES) SHOULD BE OBSERVERED FOR 10 DAYS. The local health agency with jurisdiction where the involved animal is kept will arrange confinement of the animal for observation of signs of rabies. If the animal exhibits clinical signs compatible with rabies (fever, abnormal behavior, and neurologic impairment) during confinement, it should be immediately evaluated by a veterinarian and euthanized for rabies testing, based on the veterinarian's assessment. The exposed individual can start rabies post-exposure prophylaxis, prior to completion of rabies testing in high risk situations or when testing is delayed.

- **<u>Dogs and cats showing signs of rabies at the time of the bite</u>** (i.e., unprovoked aggression, impaired locomotion, varying degrees of paralysis, extreme depression, et al.) should be evaluated immediately by a veterinarian and euthanized for testing if indicated. Begin prophylaxis of the exposed individual with HRIG and vaccine, if rabies is suspected; prophylaxis can be discontinued if test results are negative.

  Note: There is no law mandating that the owner of a suspect rabid dog or cat must euthanize their pet for rabies testing. If the owner refuses to sacrifice an ill animal, prophylaxis should be started on the exposed individual and continued as indicated. If the animal does have rabies it will usually die within 1 week and it can then be tested for rabies and the patient's prophylaxis discontinued if the animal is negative. If the animal lives 10 days following the bite, the patient's prophylaxis can be discontinued as the animal in question does not have rabies.

NO - Animal Not Available

If the animal had signs of rabies at the time of the bite (as described above), immediately begin prophylaxis of the exposed individual.

- **If the animal did not have signs of rabies**, take up to five days to attempt to find the animal, with assistance of local animal control. If found, the dog or cat in question should be confined and observed for 10 days from the date of the exposure. If the animal is not found in five days, prophylaxis should be considered. Although rabies in domestic pets is rare, prophylaxis is generally recommended for individuals with a bite exposure from a dog or cat, which cannot be observed or tested. Prophylaxis is highly recommended for bites from stray or feral cats, which cannot be observed. The physician and patient should take into account the behavior and general health status of the animal, and the circumstances of the exposure (i.e., was the animal provoked?) when making these types of prophylaxis decisions.

4. Is the bat, raccoon, skunk, fox or groundhog available for laboratory examination?

YES -The animal should be euthanized and tested for rabies. If the test is positive, administer rabies post-exposure prophylaxis. If testing of the animal is delayed more than 3 days, initiate prophylaxis with HRIG and vaccine prior to completion of testing. In the case of bites to the face, neck or fingers from animals likely to be rabid (all symptomatic bats, raccoons, skunks, foxes or groundhogs), prophylaxis should be initiated as soon as possible. Prophylaxis can be discontinued if laboratory tests results are negative.

NO - Bats, raccoons, skunks, foxes, woodchucks (groundhogs), and other carnivorous wildlife that cannot be tested, should be considered rabid. Initiate prophylaxis as soon as possible.

With regard to bat situations, post-exposure prophylaxis should be considered when direct contact between a human and a bat has occurred, unless the exposed person can be certain a bite, scratch or mucous membrane exposure did not occur. In instances in which a bat is found indoors and there is no history of bat-human contact, the likely effectiveness of post-exposure prophylaxis must be balanced against the low risk such exposures appear to present. In this setting, post-exposure prophylaxis can be considered for persons who were in the same room as the bat and who might be unaware that a bite or direct contact had occurred (e.g., a sleeping person awakens to find a bat in the room or an adult witnesses a bat in the room with a previously unattended child, mentally disabled person, or intoxicated person) and the bat is unavailable for testing. Post-exposure prophylaxis would not be warranted for other household members.

5. Is this a healthy rodent (other than a groundhog) or lagomorph (rabbit) that has lived in an indoor cage all of its life?

YES - No prophylaxis or testing is needed.

NO - Prophylaxis or testing in the case of bites from wild or outside-caged rodents and lagomorphs is rarely necessary, but might be considered in situations of unprovoked attacks by animals that exhibit bizarre aggressive behavior or obvious neurologic illness.

In the current rabies enzootic, a significant number of groundhogs have been found to be rabid. For this reason groundhogs are treated as high-risk animals (Section 4, above), despite the fact that they are rodents.

The following paragraph is from the ACIP Recommendations (1):

> "Rodents such as squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats and mice and lagomorphs, including rabbits and hares, are rarely found to be infected with rabies and have not been known to cause human rabies in the United States. Exposure to small rodents and lagomorphs hardly ever necessitates post-exposure prophylaxis.

6. There are a wide variety of other wild and domestic mammals in the State.

Livestock, ferrets, monkeys and all other mammals not listed above are also susceptible to rabies. Healthy livestock animals, which have bitten a human, are put under rabies observation for a period of 10 days. Ferrets that have bitten people can now also be observed for a period of 10 days. Monkey and other wild and exotic animal bites need to be evaluated on an individual basis. Please contact your local health department or the Department of Health and Senior Services for assistance in determining the appropriate course of action in these situations.

Bites by reptiles, fish, and birds carry no risk of rabies transmission, since rabies is a disease of mammals only.

HOW SHOULD OUT-OF-STATE BITES BE HANDLED?

Raccoon rabies is enzootic in the south, the Mid-Atlantic, and the New England regions. All high-risk animal bites (e.g., raccoon, skunk, fox, or groundhog) occurring in these states should be considered rabies exposures and prophylaxis initiated as soon as possible. Bat rabies is enzootic throughout North America and all bat exposures should be treated as soon as possible.

If the biting animal is a cat, dog, or livestock animal, which is available for observation, this can be arranged through New Jersey health officials in cooperation with local officials in the

involved state. In other cases, information on the incidence of rabies in specific species in the state where the exposure occurred and other factors will need to be taken into account. Please contact the Infectious and Zoonotic Disease Program for information and assistance with these cases at (609) 588-3121 or 588-7500. Department on-call staff can be reached during nights, weekends, and holidays by calling (609) 392-2020.

HOW CAN ANIMALS BE TESTED FOR RABIES?

Specific procedures are in place for testing animal specimens for rabies. Contact local health departments for information about laboratory testing. If testing of the animal is delayed (i.e., over weekends and holidays) in high-risk situations, the treating physician may choose to initiate post-exposure prophylaxis prior to completion of testing. In the event the test is negative, prophylaxis can be discontinued.

HOW SOON MUST POST-EXPOSURE PROPHYLAXIS BE STARTED AFTER AN EXPOSURE?

In general, post-exposure prophylaxis should be initiated as soon as possible after a decision is made to treat.

1. High Risk Situations: In cases of bites to the fingers, face or neck from high-risk animals (i.e., all symptomatic bats, raccoons, skunks, foxes, and groundhogs), prophylaxis should be initiated immediately. Post-exposure prophylaxis can always be stopped if the animal is tested and determined to be free of rabies. Prophylaxis should be started if the animal is asymptomatic but testing will not be able to be completed on a timely basis (often the case with weekend exposures).

   All bites from suspect rabid animals to immunosuppressed individuals should be treated immediately.

2. Low risk situations: Generally, delays of several days are acceptable while waiting for an animal to be located and tested, up to five days pending search for a healthy-appearing dog or cat, or up to 10 days if a healthy dog or cat is being confined for observation (4).

Post-exposure prophylaxis should be given even if long delays have occurred since exposure, as therapy may still be effective. HRIG and HDCV have prevented rabies in eight persons treated seven days after an attack by a rabid dog in Iran (5). In addition, the average time from exposure to prophylaxis in the U.S.A. in 1980 and 1981 was five days with no rabies cases resulting in treated individuals (6).

WHAT IS THE RABIES POST-EXPOSURE PROPHYLAXIS SCHEDULE?

Post-exposure prophylaxis begins with a thorough flushing and cleansing of the wound using water and soap.

Following this, a complete course (one dose of HRIG and five 1-ml doses of vaccine) is necessary for adequate prophylaxis. **This protocol should not be modified.**

1. HRIG - Administer intramuscularly (IM) only once on day 0. If not available, HRIG can be given through the seventh day of treatment. Earlier is better to provide passive protection until an antibody response to the rabies vaccine develops. The dose is 20 IU/KG or 9 IU/LB. HRIG is currently available in two and ten milliliter (ml) vials with a concentration of 150 IU per ml. At this concentration, the dose is 0.133 ml/kg or 0.06 ml/lb of body weight. Always check the package to be sure that there have been no changes in the concentration. As much as possible of the full dose should be infiltrated into and around the wound(s), and the remainder administered intramuscularly at an anatomical site distant from the vaccine. Do not give more than the recommended amount of HRIG since this may affect the immune response to the vaccine.

2. Vaccine - Administer 1.0 ml of human diploid cell vaccine (HDCV) or purified chick embryo cell culture (PCEC) vaccine IM on days 0, 3, 7, 14, and 28 into the deltoid muscle in children and adults. In infants and small children it may be preferable to give the vaccine in the midlateral aspect of the thigh. All doses must be given. Vaccine should never be given in the buttocks, since two prophylaxis failures have been documented when the vaccine was given in this manner (3).

   Note: Rabies vaccine and immune globulin should never be given together at the same body site.

HOW IS POST-EXPOSURE PROPHYLAXIS ADMINISTERED TO A PREVIOUSLY VACCINATED INDIVIDUAL?

Any person who has received the full three dose pre-exposure series of HDCV, rabies virus adsorbed (RVA) or PCEC; the full post-exposure prophylaxis with HDCV, RVA or PCEC; or has had a previous vaccination with any other type of rabies vaccine and had a documented history of antibody response to the previous vaccination needs only two doses of vaccine (days 0 and 3) when exposed to rabies. **Do not give HRIG to previously vaccinated persons**. Persons who have received rabies immunizations other than that described above should contact the Department's Infectious and Zoonotic Disease Program for guidance.

WHERE CAN THE RABIES BIOLOGICS BE OBTAINED?

All hospital emergency rooms should be prepared to provide rabies post-exposure prophylaxis. Please encourage your hospital pharmacy to stock the biologics. Human rabies vaccines are available through pharmaceutical vendors or directly though the manufacturers.

- Human diploid cell vaccine (IMMOVAX Rabies) can be ordered from Sanofi Pasteur, telephone number (800) 822-2463 (800 VACCINE), http://www.imovax.com.
- Purified chick embryo cell culture (RabAvert) can be ordered from Chiron Corp., telephone number (800) 244-7668, (800 Chiron8), http://www.novartisvaccines.com/products/travel.shtml .
- Human rabies immune globulin (HRIG) is available from both Sanofi Pasteur (IMOGAM RABIES-Ht) telephone number (800) 822-2463 (800 VACCINE), http://www.imovax.com. and Talecris Biotherapeutics (HyperRAB), telephone number (800) 243-4153 or (800) 520-2807, http://www.talecrisusa.com/prod_hype_brab.asp

Please contact the New Jersey Department of Health and Senior Services, Infectious and Zoonotic Disease Program at (609) 588-3121 or 588-7500, if problems arise in securing the appropriate rabies biologics in a timely manner.

WHAT ARE THE SIDE EFFECTS OF POST-EXPOSURE PROPHYLAXIS?

HRIG is a human immune globulin and has the same excellent safety profile as other human immune globulins. There is no evidence that hepatitis B virus (HBV) human immunodeficiency virus (HIV) or other viruses have ever been transmitted by commercially available HRIG available in the United States. Local pain and low-grade fever may follow receipt of HRIG.

The following discussion of adverse reactions to HDCV is from the ACIP Recommendations (1):

> "Reactions after vaccination with HDCV are less common than with previously available vaccines. In a study using a three-dose post-exposure regimen of HDCV, local reactions, such as pain, erythema, and swelling or itching at the injection site, were reported among 30 to 70 percent of recipients of HDCV, and mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness were reported among 5 to 40 percent of recipients. Three cases of neurologic illness resembling Guillain-Barre syndrome that resolved without sequelae in 12 weeks have been reported.
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> An immune complex-like reaction occurs among approximately six percent of persons receiving booster doses of HDCV 2 to 21 days post booster. These patients developed a generalized urticaria sometimes accompanied by arthralgia, arthritis, angioedema, nausea, vomiting, fever and malaise. In no cases have the illnesses been life threatening. This reaction occurs much less frequently among persons receiving primary immunization."

Significant adverse reactions should be reported to the vaccine manufacturer. If a person experiences an adverse reaction to HDCV, the physician should consider completing the prophylaxis with another human rabies vaccine (i.e. RVA or PCEC). Discontinuance of post-exposure prophylaxis is usually not indicated, even in cases of severe reactions. Contact the vaccine manufacturer or the New Jersey Department of Health and Senior Services, Infectious and Zoonotic Disease Program, if additional guidance is needed.

WHO SHOULD RECEIVE PRE-EXPOSURE VACCINATION?

It is recommended that veterinarians, veterinary technicians, animal control officers, shelter workers, persons who will be preparing rabies specimens, and persons working closely with high risk wildlife species consider receiving pre-exposure rabies vaccinations.

Pre-exposure vaccination consists of the administration of 1.0 ml human rabies diploid cell vaccine (HDCV) or purified chick embryo cell culture (PCEC) intramuscularly on days 0, 7, and 21 or 28.

Note: Persons who have received the complete post-exposure prophylaxis series are considered previously vaccinated for any future exposures.

Although antibody levels do not define a person's immune status, they are a marker of continuing immune response. To ensure the continuity of an immune response, titers should be checked periodically, with booster doses administered as needed. Persons in the frequent-risk category (rabies lab workers, animal control and wildlife workers, and veterinarians and their staff in rabies enzootic areas) should have a serum sample tested every 2 years to determine if an adequate antibody level persists. If their antibody titer is below the 1:5 serum dilution by RFFIT, a booster dose of vaccine should be given.

Any person with a history of pre-exposure vaccination with HDCV, RVA, or PCEC; prior post-exposure prophylaxis with HDCV, RVA, or PCEC; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination are considered vaccinated and would only need 2 booster vaccinations, 3 days apart.

REFERENCES

1. Centers for Disease Control, Rabies Prevention - United States, 1999: Recommendations of the Advisory Committee Immunization Practices (ACIP), MMWR 1999;48 (No. RR-1):1-21.

2. Austin C., Scientific Reports: Zoonoses Update Bats and Rabies, JAVMA, 1998,213:1323-1325.

3. Centers For Disease Control, Human Rabies Despite Prophylaxis With Rabies Immune Globulin and Human Diploid Cell Rabies Vaccine - Thailand, MMWR, 1987:36:36:759765.

4. Fishbein D.B., Arcangeli S., Rabies Prevention in Primary Care. Postgraduate Medicine, 1987:82(3):83-95.

5. Bahmanyer M., Fayax A., Shokrollak N., et al, Successful Protection of Humans Exposed to Rabies Infection, Post-exposure Prophylaxis With the New Human Diploid Cell Rabies Vaccine and Antirabies Serum, JAMA, 19976:235(24):2751-2754.

6. Helmick, C.G., The Epidemiology of Human Rabies Post-exposure Prophylaxis, 1980-1981, JAMA 1983:250(15):1990-1996.